waveform to accurately match the aortic waveform (Figure), and (ii) preload reduction achieved with phase I of Valsalva maneuver (VM). In 10 normal healthy male subjects aged 34.7 ± 5.8 (mean ± SD), we studied the reproducibility of this system during four consecutive preload reduction runs.

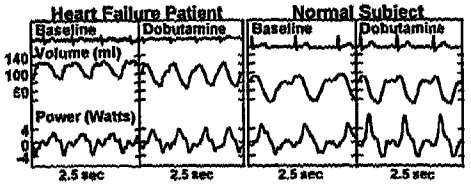
Results: VM reduces preload (end diastolic area: from 12.7 ± 1.8 to 10.3 ± 1.6 cm^2, $p < 0.001$, ANOVA), end systolic pressure (from 99.1 ± 14.8 to 89.7 ± 17.5 mmHg, $p < 0.001$) and LV work (stroke force: from 653.0 ± 165.3 to 454.6 ± 117.0 mmHg.cm^2, $p < 0.001$). Of the two measures of LV systolic function, the end systolic pressure-area relationship was highly nonlinear (r^2: 0.54 ± 0.28 vs 0.87 ± 0.17, $p < 0.001$) and exhibited higher variability (SD/mean) than the stroke force-end diastolic area relationship for both slope (0.31 vs 0.11) and intercept (0.46 vs 0.22).*Conclusion:* This totally non-invasive method should be useful in assessing the systolic LV function repeatedly in clinical settings.

11:45

708-6 Preload-Adjusted Maximal Power Using Echocardiographic Automated Border Detection to Assess Left Ventricular Function

Christine M. Mahler, William E. Katz, Srinivas Murali, Marc D. Feldman, John Gorcsan III. *University of Pittsburgh, Pittsburgh, PA*

Preload-adjusted maximal power (PAMP) has recently been validated as a load insensitive measure of LV function. The objective was to estimate PAMP in pts with severe congestive heart failure (CHF) and normal subjects using automated echocardiographic LV volume and simultaneous noninvasive arterial pressure. Ten CHF pts, aged 45 ± 10 yrs, (LVEF 21 ± 6%) and 10 normal subjects, aged 32 ± 3 yrs, (LVEF 56 ± 5%) were studied at baseline and with 10 μg/kg/min dobutamine infusion. LV volume by 4-chamber view Simpson's rule and arterial pressure by a finger cuff photoplethysmograph were acquired on-line. The first derivative of LV volume was multiplied by pressure to estimate maximal LV power, then adjusted by dividing by end-diastolic volume squared. Volume and power examples are shown.



Baseline PAMP was 0.84 ± 0.63 W/ml^2 in CHF pts vs. 4.18 ± 1.64 W/ml^2 in normals ($p < 0.001$). PAMP increased with dobutamine to 1.55 ± 1.56* in CHF pts and 8.39 plusmn; 3.73# W/ml^2 in normals (*$p < 0.05$ vs. baseline & normal, #$p < 0.001$ vs. baseline). PAMP using echo automated border detection has potential to assess LV function.

709 Molecular Analysis of Left Ventricular Hypertrophy and Remodeling

Monday, March 25, 1996, 10:30 a.m.–Noon
Orange County Convention Center, Room 222

10:30

709-1 Echocardiographic Assessment of Left Ventricular Systolic Function in Transgenic Mice With Cardiac Specific Over-Expression of Phospholamban

Brian D. Holt, Zia U. Khan, Nancy Ball, Vivek J. Kadambi, Evangelia G. Kranias, Richard A. Walsh. *University of Cincinnati, Cincinnati, OH*

In vitro studies have demonstrated that dephosphorylated phospholamban (PLB) is an inhibitor of the cardiac sarcoplasmic reticulum (SR) calcium ATPase (Ca^{2+} ATPase), and that phosphorylation of this protein by catecholamine-mediated stimulation of cyclic AMP-dependent protein kinase relieves this inhibition and facilitates reuptake of calcium by the SR. To determine the effects of PLB on *in vivo* LV systolic function and assess the stoichiometry between PLB and the SR Ca^{2+} ATPase, 15 transgenic mice with cardiac specific overexpression of phospholamban (PLBOE) driven by the α-myosin heavy chain promoter, and 16 wildtype age-matched controls (CON) were studied under light anesthesia with 2D-directed M-mode and Doppler using a 9 MHz imaging and 5–7.5 MHz Doppler transducer (Interspec-ATL CX 200). LV shortening fraction (SF), heart rate-corrected velocity of circumferential shortening (Vcf_c), peak aortic velocity (AoV) and mean aortic acceleration (Acc) were compared at baseline (BASE) and after intraperitoneal isoproterenol (ISO) injection (2 μg/gm):

	CON		PLBOE	
	BASE	ISO	BASE	ISO
HR (bpm)	292 ± 87	452 ± 69*	280 ± 98	431 ± 95*
SF (%)	44 ± 5	66 ± 5*	35 ± 6†	64 ± 4*
Vcf_c (circ/s)	6.2 ± 1.9	11.5 ± 2.1*	4.2 ± 1.0†	10.4 ± 2.1*
AoV (cm/s)	71.3 ± 12.9	88.5 ± 17.7*	66.5 ± 8.4	92.5 ± 13.0*
Acc (m/s^2)	3.7 ± 1.5	6.0 ± 2.2*	2.9 ± 0.9	6.5 ± 1.6*

Data are mean ± SD; *$p < 0.05$ vs. BASE, †$p < 0.05$ vs. CON

With ISO, the percent increase in SF, Vcf_c and mean acceleration were significantly greater in PLBOE than CON. We conclude that overexpression of phospholamban: 1) decreases basal LV systolic function, indicating that a fraction of the sarcoplasmic reticulum Ca^{2+} ATPase in wildtype mice is not under regulation by phospholamban, and 2) enhances inotropic, but not chronotropic sensitivity to β adrenergic stimulation.

10:45

709-2 Rapid Coordinate Upregulation of Nuclear and Mitochondrial Gene Expression in Response to Cardiac Load

Gregg T. Schuyler, Terrence X. O'Brien, John D. Rozich, Robert L. Kent, Diane E. McDermott, Paul J. McDermott, George Cooper IV, Donald R. Menick. *Gazes Cardiac Research Institute and Med. Univ. of SC, Charleston, SC 29425*

To identify important transcripts upregulated during acute right ventricular (RV) pressure overload in the adult cat, differential hybridization was utilized. A modified Swan-Ganz catheter was used to partially obstruct the RV outflow, under flouroscopy, creating a RV pressure overload. The balloon was positioned such that the systemic pressure was unchanged resulting in a same animal control normally loaded left ventricle (LV). cDNA libraries construced from RV and LV were differentialy hybridized to select for clones present in the RV but absent in the LV. One upregulated clone, confirmed by Northern blot hybridization, corresponded to the mitochondrial F_1 ATPase subunit Fo_8 whose sequence is encoded in the mitochondrion (Mt). This upregulation was also demonstrated in related Mt encoded transcripts, cytochrome *b* and cytochrome oxidase subunit II. To demonstrate a coordinate upregulation of mitochondrial respiratory proteins which are encoded in the nucleus, the levels of transcripts of cytochrome C, cytochrome oxidase subunit IV, and mitochondrial RNA processing RNA were analyzed. Again a rapid upregulation in response to acute hemodynamic load was observed. This *in vivo* effect was then tested *in vitro* in isolated neonatal rat ventricular cardiocytes treated with phenylephrine (PE) stimulation. Similar changes in the mRNA levels were seen after 1–2 hr. At the protein level, Western analysis of cytochrome *c* showed a significant increase within 3 days of PE stimulation. Additionally, to correlate the neonatal cell studies with adult cells, feline adult cardiocytes were stretched for 1 hour on a deformable membrane, with similar results. These studies suggest both *in vivo* and *in vitro*, a cardiac regulatory mechanism that responds to hypertrophic stimuli with a rapid *coordinate* upregulation of nuclear and mitochondrial genes encoding the oxidative phosphorylation components.

11:00

709-3 Determinants of the Variability of Left Ventricular Hypertrophy in Patients With Hypertrophic Cardiomyopathy

Winifred Kelsey, Antoine Abchee, Marcel Lechin, Robert Roberts, Ali J. Marian. *Baylor College of Medicine, Houston, TX*

The hallmark of phenotypic expression of Hypertrophic cardiomyopathy (HCM) is left ventricular hypertrophy (LVH). However, the magnitude and extent of LVH in patients with HCM, even in those with the same underlying mutation, are variable. A number of genetic and environmental factors are likely to influence the phenotypic expression of LVH in patients with HCM. We have previously shown that ACE genotypes account for 5–10% of the variability of the extent and magnitude of LVH in patients with HCM. In this study we determined the influence of gender, age, height, weight, body mass index, angiotensinogen (AGT) genotypes T174M, and M235T, angiotensin II receptor Ia (ATR1a) genotypes on left ventricular mass index (LVMI) calculated by area-lenghth method, and extent of hypertrophy determined using a semiquantitative point score (Score 1–10). Multiple regression analysis showed that only gender and ACE genotypes were correlated with LVMI and extent of LVH. LVMI was greater in male (n = 61) than in female (n-47) patients with HCM (145.96 ± 34 vs. 129.42 ± 33, $p = 0.013$). Similarly, male patients had more extensive hypertrophy than female patients (socre 6.4 ± 2.2 vs. 5.3 ± 1.9, $p = 0.009$). Gender accounted for 4.8% and 5.4% of the

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